

**WHAT IS CLAIMED IS:**

1. A method of creating a chemical compound library comprising:
  - 5 selecting compounds having a molecular weight of no greater than about 350 grams/mole; and
  - selecting compounds having a solubility in deuterated water of at least about 1 mM at room temperature.
- 10 2. The method of claim 1 wherein a majority of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 15 3. The method of claim 2 wherein all of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 20 4. The method of claim 1 wherein the compounds selected have a molecular weight of no greater than about 325 grams/mole.
5. The method of claim 4 wherein the compounds selected have a molecular weight of less than about 325 grams/mole.
- 25 6. A chemical compound library comprising compounds having a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 30 7. The library of claim 6 wherein a majority of the compounds have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
8. The library of claim 7 wherein all of the compounds have a molecular

weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.

9. The library of claim 6 wherein the compounds have a molecular weight of no greater than about 325 grams/mole.
10. The library of claim 9 wherein the compounds have a molecular weight of less than about 325 grams/mole.
- 10 11. A method of identifying a lead chemical template, the method comprising:
  - selecting compounds having a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature to create a chemical compound library;
  - 15 identifying at least one compound from the library that functions as a ligand to a target molecule having a dissociation constant of at least about 100  $\mu$ M; and
  - using the ligand to identify a lead chemical template.
- 20 12. The method of claim 11 wherein a majority of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 25 13. The method of claim 12 wherein all of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 30 14. The method of claim 11 wherein the compounds selected have a molecular weight of no greater than about 325 grams/mole.
15. The method of claim 14 wherein the compounds selected have a

molecular weight of less than about 325 grams/mole.

16. The method of claim 11 wherein the dissociation constant of a lead chemical template to the target molecule is at least about 1  $\mu$ M.  
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17. The method of claim 11 wherein the target molecule is a protein.
18. A method of identifying a compound that binds to a target molecule, the method comprising:
  - 10 providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;  
introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;  
providing a nuclear magnetic resonance spectrometer equipped
  - 15 with a flow-injection probe;  
transferring each test sample from the sample reservoir into the flow-injection probe;  
collecting a relaxation-edited nuclear magnetic resonance spectrum on each sample in each reservoir; and
  - 20 comparing the spectra of each sample to the spectra taken under the same conditions in the absence of the target molecule to identify compounds that bind to the target molecule;  
wherein the concentration of target molecule and each compound in each sample is no greater than about 100  $\mu$ M.  
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19. The method of claim 18 wherein each mixture is in a sample reservoir of a multiwell sample holder.
20. The method of claim 19 wherein the multiwell sample holder is a 96-well  
30 microtiter plate.
21. The method of claim 18 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

22. The method of claim 18 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.

5 23. The method of claim 18 wherein collecting a relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited nuclear magnetic resonance spectrum.

10 24. The method of claim 23 wherein collecting a 1D relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited  $^1\text{H}$  nuclear magnetic resonance spectrum.

15 25. The method of claim 18 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.

26. The method of claim 25 wherein the mixture of compounds comprises at least about 6 compounds.

20 27. The method of claim 25 wherein the ratio of target molecule to each test compound in each sample reservoir is about 1:1.

25 28. The method of claim 18 wherein the concentration of target molecule and each compound in each sample is no greater than about 50  $\mu\text{M}$ .

29. The method of claim 18 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100  $\mu\text{M}$ .

30 30. The method of claim 18 wherein the target molecule is a protein.

31. A method of identifying a compound that binds to a target molecule, the method comprising:  
providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;

introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

5       transferring each test sample from the sample reservoir into the flow-injection probe;

      collecting a WaterLOGSY nuclear magnetic resonance spectrum on each sample in each reservoir; and

      analyzing the spectra of each sample to distinguish binding

10      compounds from nonbinding compounds by virtue of the opposite sign of their water-ligand NOEs.

32.     The method of claim 31 wherein the concentration of target molecule is no greater than about 10  $\mu$ M.

15      33.    The method of claim 32 wherein the concentration of target molecule is no greater than about 1  $\mu$ M.

      34.    The method of claim 31 wherein the concentration of each compound in

20      each sample is no greater than about 100  $\mu$ M.

      35.    The method of claim 31 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

25      36.    The method of claim 31 wherein each mixture is in a sample reservoir of a multiwell sample holder.

      37.    The method of claim 36 wherein the multiwell sample holder is a 96-well microtiter plate.

30      38.    The method of claim 31 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.

39. The method of claim 38 wherein each test compound has a molecular weight of no greater than about 325 grams/mole.

40. The method of claim 31 wherein collecting a WaterLOGSY nuclear magnetic resonance spectrum comprises collecting a 1D WaterLOGSY nuclear magnetic resonance spectrum.

41. The method of claim 31 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.

42. The method of claim 41 wherein the mixture of compounds comprises at least about 6 compounds.

43. The method of claim 31 wherein the ratio of target molecule to each test compound in each sample reservoir is about 10:1.

44. The method of claim 31 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100  $\mu$ M.

45. The method of claim 31 wherein the target molecule is a protein.